```
=> d hist

     (FILE 'HOME' ENTERED AT 11:04:38 ON 16 MAY 2003)

     FILE 'REGISTRY' ENTERED AT 11:04:48 ON 16 MAY 2003
L1           317 S CD40
L2             0 S CD40/CN
L3          1617 S ?STATIN

     FILE 'CAPLUS, MEDLINE, BIOSIS' ENTERED AT 11:08:57 ON 16 MAY 2003
L4         18891 S ATORVASTATIN OR LOVASTATIN OR PRAVASTATIN OR FLUVASTATIN OR M
L5        627473 S INFLAMMAT?
L6           823 S L4 AND L5
L7           275 S L6 AND (IMMUN? OR AUTOIMMUN?)
L8            76 S L7 AND ATORVASTATIN
L9            10 S L8 AND AUTOIMMUN?
L10            6 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)
L11           66 S L8 NOT L9
L12           48 DUPLICATE REMOVE L11 (18 DUPLICATES REMOVED)
L13          283 S L6 AND PY<=2000
L14           41 S L13 AND ATORVASTATIN
L15           26 DUPLICATE REMOVE L14 (15 DUPLICATES REMOVED)
L16           26 S L4 AND ARTHRITIS
L17            5 S L16 AND ATORVASTATIN
L18            5 DUPLICATE REMOVE L17 (0 DUPLICATES REMOVED)

=> s l16 not l17
L19           21 L16 NOT L17
```

WEST

Help | Logout | Interrupt

Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences | Cases

Search Results -

Terms	Documents
5633246	3

Database:
- US Patents Full-Text Database
- US Pre-Grant Publication Full-Text Database
- JPO Abstracts Database
- EPO Abstracts Database
- Derwent World Patents Index
- IBM Technical Disclosure Bulletins

Search: L10

Refine Search

Recall Text | Clear

Search History

DATE: Friday, May 16, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=AND			
L10	5633246	3	L10
L9	l6 not diabetes	72	L9
L8	L6 and atorvastatin.clm.	39	L8
L7	L6 and atorvastatin	241	L7
L6	L4	573	L6
DB=JPAB,EPAB,DWPI; PLUR=YES; OP=AND			
L5	L4	39	L5
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=AND			
L4	L3 and l2	1079	L4
L3	diabetes or multiple adj sclerosis or rheumatoid adj arthritis or crohne or lupus adj erythematosus	73071	L3
L2	atorvastatin or lovastatin or pravastatin or fluvastatin or mevastatin or cerivastatin or rosuvastatin or simvastatin	2926	L2
DB=USPT; PLUR=YES; OP=AND			
L1	atorvastatin or lovastatin or pravastatin or fluvastatin or mevastatin or cerivastatin or rosuvastatin or simvastatin	1539	L1

END OF SEARCH HISTORY

WEST

Generate Collection Print

L5: Entry 24 of 39 File: DWPI Sep 28, 2000

DERWENT-ACC-NO: 2000-611600
DERWENT-WEEK: 200216

TITLE: Increasing endothelial cell nitric oxide synthase activity in non-hypercholesterolemic subject, useful for treating e.g. pulmonary hypertension and ischemic stroke, comprises administering HMG-CoA reductase inhibitor, e.g. lovastatin

INVENTOR: ENDRES, M; LAUFS, U ; LIAO, J K ; MOSKOWITZ, M A

PATENT-ASSIGNEE:

ASSIGNEE	CODE
BRIGHAM & WOMENS HOSPITAL INC	BGHM

PRIORITY-DATA: 1999US-0273445 (March 19, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200056403 A1	September 28, 2000	E	066	A61P009/10
EP 1175246 A1	January 30, 2002	E	000	A61P009/10
AU 200037603 A	October 9, 2000		000	A61P009/10

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
WO 200056403A1	March 17, 2000	2000WO-US07221	
EP 1175246A1	March 17, 2000	2000EP-0916511	
EP 1175246A1	March 17, 2000	2000WO-US07221	
EP 1175246A1		WO 200056403	Based on
AU 200037603A	March 17, 2000	2000AU-0037603	
AU 200037603A		WO 200056403	Based on

INT-CL (IPC): A61 P 9/10

RELATED-ACC-NO: 2000-611598

ABSTRACTED-PUB-NO: WO 200056403A
BASIC-ABSTRACT:

NOVELTY - Use of HMG-CoA reductase inhibitors (I) as upregulators of endothelial cell nitric oxide synthase (ecNOS) is new.

DETAILED DESCRIPTION - Increasing endothelial cell nitric oxide synthase (ecNOS)

activity in a non-hypercholesterolemic subject who would benefit from increased ecNOS activity comprises administering an HMG-CoA reductase inhibitor (I).

INDEPENDENT CLAIMS are also included for the following:

(1) increasing ecNOS activity in a subject to treat a non-hyperlipidemic condition favorably affected by an increase in ecNOS activity in a tissue comprising administering (I);

(2) reducing brain injury resulting from a stroke, comprising administering (I) to a subject having an abnormally high risk of an ischemic stroke, to increase ecNOS activity in the brain tissue of the subject;

(3) treatment of pulmonary hypertension comprising administering (I) to increase cell NOS activity in the pulmonary tissue of the subject, provided that (I) is not an HMG-Co A reductase inhibitor (sic);

(4) treating heart failure comprising administering (I) to increase ecNOS activity in the heart tissue of the subject, provided that (I) is not a rho GTPase function inhibitor;

(5) treating progressive renal disease comprising administering (I) to increase ecNOS activity in the kidney tissue of the subject, provided that (I) is not a rho GTPase function inhibitor;

(6) increasing blood flow in a tissue of a subject comprising administering (I) to increase ecNOS activity in the tissue;

(7) screening for identifying (I) for treating subjects who would benefit from increased ecNOS activity in a tissue comprising: (a) identifying (I) suspected of increasing ecNOS activity; and (b) determining whether or not the (I) produces an increase in ecNOS activity in vivo or in vitro;

(8) a pharmaceutical composition comprising (I) and L-arginine.

ACTIVITY - Hypotensive; vasotropic; cerebroprotective; anticoagulant; thrombolytic; cardiant; arteriosclerotic; immunosuppressive; neuroprotective; nootropic; antirheumatic; antiarthritic; dermatological; antiinflammatory; nephrotropic.

MECHANISM OF ACTION - (I) regulate ecNOS activity other than through preventing the formation of oxidative LDL. (I) increases ecNOS activity by effects directly on endothelial rather than hepatic HMG-CoA reductase. (The upregulation of activity does not depend on a decrease in cholesterol synthesis).

USE - For increasing ecNOS levels in non-hypertriglyceridemic or non-hyperlipidemic individuals. For an individual with abnormally low level of ecNOS activity which is chemically induced; abnormally elevated risk of pulmonary hypertension or ischemic stroke, has experienced an ischemic stroke or has pulmonary hypertension; is chronically exposed to hypoxic conditions; has abnormally elevated risk of thrombosis, arteriosclerosis, myocardial infarction or reperfusion injury, or the individual has thrombosis, arteriosclerosis or has experienced a myocardial infarction. For an individual who is a transplant recipient, or has homocystinuria, neurodegenerative disease (especially Alzheimer's disease) or cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL) syndrome (all claimed). For progressive renal disease and reducing brain injury following a stroke. Conditions which can benefit from increased ecNOS activity include impotence, gastric and esophageal motility disorders, kidney disorders such as kidney hypertension and insulin deficiency; also, inflammatory diseases resulting from cytokine induced reduced levels of ecNOS activity, e.g. non-cholesterol induced atherosclerosis, transplant arterial sclerosis, rheumatoid arthritis, lupus, scleroderma and emphysema. (I) can be used acutely or prophylactically to treat conditions that result form low level of ecNOS. Treatment using (I) is excluded when the subject has an abnormally elevated risk of ischemic stroke.

Endothelial cells treated with simvastatin at 0.1 mmol/l for various duration (0-84

hours) exhibited an increase in ecNOS protein levels of 4 plus or minus 6, 21 plus or minus 9, 80 plus or minus 8, 90 plus or minus 12 and 95 plus or minus 16% after 12, 24, 48, 72 and 84 hours respectively.

ADVANTAGE - The effect of (I) on upregulation of ecNOS occurs within a few days, allowing (I) to be administered during short term increase in risk of stroke or other embolic events, such as that due to surgical intervention, even in hypercholesterolemic patients.

CHOSEN-DRAWING: Dwg.0/6

TITLE-TERMS: INCREASE ENDOTHELIUM CELL NITRIC OXIDE SYNTHASE ACTIVE NON SUBJECT USEFUL TREAT PULMONARY HYPERTENSIVE STROKE COMPRISE ADMINISTER COENZYME=A REDUCTASE INHIBIT

DERWENT-CLASS: B05

CPI-CODES: B04-J02; B06-D01; B07-A02B; B07-D02; B07-D04; B10-A17; B10-C04A; B11-C08E2; B12-K04E; B14-C03; B14-C06; B14-C09B; B14-D10; B14-F01; B14-F02B; B14-F02C; B14-F02D; B14-F04; B14-F07; B14-G02; B14-J01; B14-J01A4; B14-N17; B14-N17B;

CHEMICAL-CODES:

Chemical Indexing M2 *01*
Fragmentation Code
F012 F013 F014 F015 F016 F431 G013 G100 H4 H402
H482 H5 H581 H6 H601 H641 H7 H721 H8 J0
J011 J1 J171 M1 M113 M210 M211 M213 M232 M240
M272 M281 M282 M311 M315 M321 M332 M342 M344 M371
M373 M391 M413 M431 M510 M521 M531 M540 M750 M782
M904 M905 N102 P420 P421 P423 P433 P520 P522 P526
P527 P528 P616 P617 P813 P814 P942 P943
Specfic Compounds
A00PDK A00PDT A00PDA A00PDM

Chemical Indexing M2 *02*
Fragmentation Code
F011 F012 F013 F014 F015 F016 F017 F019 F123 F421
G010 G013 G019 G100 H1 H181 H2 H201 H4 H401
H421 H6 H601 H641 H8 J0 J011 J3 J311 J5
J521 L9 L942 M1 M113 M119 M123 M136 M210 M213
M232 M240 M281 M312 M321 M332 M342 M373 M391 M413
M431 M510 M522 M533 M540 M750 M782 M904 M905 N102
P420 P421 P423 P433 P520 P522 P526 P527 P528 P616
P617 P813 P814 P942 P943
Specfic Compounds
A06ALK A06ALT A06ALA A06ALM

Chemical Indexing M2 *03*
Fragmentation Code
D014 D601 G013 G100 H1 H181 H2 H201 H4 H402
H482 H6 H601 H641 H7 H721 H8 J0 J011 J1
J171 M1 M113 M210 M213 M232 M273 M281 M315 M321
M332 M344 M371 M391 M412 M431 M511 M520 M531 M540
M750 M782 M904 M905 N102 P420 P421 P423 P433 P520
P522 P526 P527 P528 P616 P617 P813 P814 P942 P943
Specfic Compounds
23348K 23348T 23348A 23348M

Chemical Indexing M2 *04*
Fragmentation Code
A111 A960 C710 G033 G034 G060 G670 H4 H403 H461
H482 H8 J0 J012 J1 J171 J2 J261 M210 M211
M214 M232 M240 M262 M281 M315 M321 M332 M344 M371
M391 M411 M431 M510 M520 M530 M541 M630 M750 M782
M904 M905 N102 P420 P421 P423 P433 P520 P522 P526

P527 P528 P616 P617 P813 P814 P942 P943
Specfic Compounds
A0S9EK A0S9ET A0S9EA A0S9EM

Chemical Indexing M2 *05*
Fragmentation Code
F012 F014 F016 F123 G033 G034 G670 H4 H401 H421
H8 J0 J011 J2 J261 J5 J521 L9 L942 M1
M126 M135 M210 M211 M214 M232 M240 M262 M281 M282
M312 M321 M332 M342 M413 M431 M510 M521 M530 M541
M750 M782 M904 M905 N102 P420 P421 P423 P433 P520
P522 P526 P527 P528 P616 P617 P813 P814 P942 P943
Specfic Compounds
16653K 16653T 16653A 16653M 19716K 19716T 19716A 19716M

Chemical Indexing M2 *06*
Fragmentation Code
F012 F014 F016 F123 G033 G034 G670 H4 H401 H402
H421 H482 H8 J0 J011 J012 J1 J171 J2 J261
J5 J521 L9 L942 M1 M126 M135 M210 M211 M215
M233 M240 M262 M281 M282 M312 M315 M321 M332 M342
M344 M371 M391 M413 M415 M431 M510 M520 M521 M530
M541 M750 M782 M904 M905 N102 P420 P421 P423 P433
P520 P522 P526 P527 P528 P616 P617 P813 P814 P942
P943
Specfic Compounds
16884K 16884T 16884A 16884M

Chemical Indexing M1 *07*
Fragmentation Code
M423 M431 M750 M782 M905 N102 P420 P421 P423 P433
P520 P522 P526 P527 P528 P616 P617 P813 P814 P942
P943
Specfic Compounds
A012OK A012OT A012OA A012OM

Chemical Indexing M2 *08*
Fragmentation Code
H1 H100 H181 J0 J011 J1 J171 K0 L2 L250
M280 M314 M321 M332 M343 M349 M381 M391 M416 M431
M620 M782 M800 M904 M905 M910 P420 P421 P423 P433
P520 P522 P526 P527 P528 P617 P813 P814 P942 P943
Specfic Compounds
04093K 04093T 04093M 04742K 04742T 04742M
Registry Numbers
1661U

UNLINKED-DERWENT-REGISTRY-NUMBERS: 1661U

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C2000-183041